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RECENT DEVELOPMENTS IN THE STUDY OF THE RELATIONSHIP BETWEEN CHEMICAL CONSTITUTION AND PHYSIOLOGICAL ACTION OF ORGANIC COMPOUNDS.

By Prof. Virgil Coblentz.

The object of this paper is to present, in as concise a manner as possible, the outline of a few selected topics bearing upon this subject. At a future date a more complete presentation of this subject will be made. Those interested in modern synthetics will find a general résumé of the subject in the *Journal of the Society of Chemical Industry*, Vol. xvii, No. 8.

The long well-known fact that certain relations existed between physiological action, molecular weight and isomorphous inorganic bodies led to a similar study of organics. This subject received its direct stimulus by Fischer's discovery of Kairine in 1882, followed by the accidental discovery of the antipyretic properties of acetanilid in 1887.

A proof that a close relationship exists between chemical constitution and physiological action is shown by the fact that certain changes in chemical structure or constitution causes like changes in the physiological action of similar bodies; further, the addition of certain groups to compounds of different action produces bodies of similar physiological action or are alike rendered inactive.

According to Crum Brown and Fraser the methylating of different alkaloids of different physiological action produces compounds which paralyze all the motoric nerve terminals like curarin.

The introduction of the carboxyl (COOH) or the sulphonic acid (SO_3H) groups into bodies of well defined toxic properties, results

in a marked diminution or total disappearance of their action, as for example

Benzole C_6H_6 — Benzoic acid C_6H_5COOH

Phenol C_6H_5OH — Para-phenol sulphonic acid $C_6H_4\begin{matrix}OH\\SO_3H\end{matrix}$

Phenyl sulphonic acid $C_6H_5 - O - SO_3H$

Ortho-phenol carboxylic acid $C_6H_4\begin{matrix}OH\\COOH\end{matrix}$

Naphtalin $C_{10}H_8$ — Naphtoic acid $C_{10}H_7COOH$

Ammonia NH_3 — Glycocoll CH_2NH_2COOH

Morphin $C_{17}H_{17}\begin{matrix}OH\\NO—OH\end{matrix}$ — Morphin sulphonic acid $C_{17}H_{17}\begin{matrix}OH\\NO—SO_3H\end{matrix}$

(May be given in five times the morphin dose.)

Naphtol yellow $C_{10}H_4\begin{matrix}OH\\-(NO_2)_2\\SO_3H\end{matrix}$ — a non-toxic derivative of toxic Martiu's yellow.

It is immaterial if the sulphonic acid group is united to a carbon or oxygen.

The toxicity of the organic acids decreases with the increase of carboxyl groups, as from formic and acetic acids to tartaric and citric acids. The toxic characters of oxalic acid $[(COOH)_2]$ are due to the double

$$\left(\begin{matrix}Co\\|\\Co\end{matrix}\right)$$

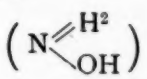
carboxyl group which in effect resembles the dicyanogen

$$\left(\begin{matrix}Cn\\|\\Cn\end{matrix}\right)$$

The stability of the carboxyl and sulphonic acid groups serves to protect these derivatives from breaking up in the system and exerting toxic action. That certain groups lose their specific action through simple changes in the molecular structure is explained physiologically in that certain cell groups of the organism exert a

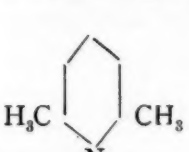
selective influence upon exposed groups of the molecule, thereby anchoring the entire complex in certain tissues where they break up and exert their action. This is especially noticeable through changing terminal or exposed groups when the action fails entirely, although the nucleus remains intact.

The theory of Loew,[1] which aims to explain the chemical constitution of living protoplasm, claims that all substances which in great dilution react with aldehyde or amido groups, are toxic to all forms of life, and the greater the reactive ability of a substance with reference to these groups, the greater its activity and toxicity. Such bases as hydroxylamine



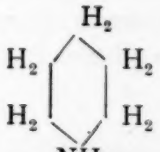
and diamid $H_2N - NH_2$ which react readily with aldehydes and ketones are active poisons for plants and animals. Phenylhydrazine ($C_6H_5NH - NH_2$), which is especially reactive towards aldehydes ($R - CHO$), and the Keto ($R - CO - R$) groups is on the same ground a violent blood poison.

Bodies containing a tertiary nitrogen and possessing slight or no toxic properties, become very poisonous through reduction and formation of an imido group.



Collidin

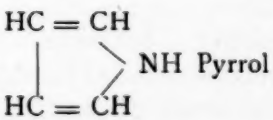
Pyridin



Piperidin

Thus pyridin is more toxic than collidin, and piperidin more than either of the others.

Tetrahydro quinolin is far more energetic than quinolin, likewise pyrrol

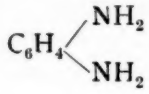


Pyrrol

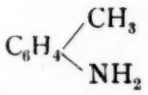
is more poisonous than pyridin.

[1] Die chemische Energie der lebenden Zellen.

Loew explains this by the increase of reactive ability towards the aldehyde groups of the protoplasm. This theory is supported by the observation that bodies with labile amido groups increase in toxicity when a second amido group is introduced. This decreases, however, when the amido (NH_2 —) group is converted into an imido (— NH) group. Thus the phenylene diamines



are more toxic than



toluidin, also when one H of the amido group in anilin ($C_6H_5NH_2$) is replaced by an acid radical as acetyl (CH_3CO) or benzoyl (C_6H_5CO) as in acetanilid ($C_6H_5NHCH_3CO$) or benzanilid ($C_6H_5NHC_6H_5CO$) these bodies react less readily than anilin with aldehydes.

Our greatest difficulty is accountable to our fragmentary knowledge of the selective powers of the human organs and tissues, which has been only partially established through histological staining and toxicological experiments. Loew's views enlighten us only upon certain groups of bodies which react with aldehydes and amido groups.

INFLUENCE OF HYDROXYL GROUPS.

The introduction of hydroxyl (—OH) groups in aliphatic bodies modifies their action, which decreases with their increase in number. Thus the narcotic alcohols and aldehydes the harmless glycols, glycerols and aldols, still more marked is the change exemplified in the polyhydric alcohols, as heptol, mannitol, etc. The presence of this group in caffeine practically destroys its effect. These groups so affect the stability of a compound that its decomposition in the system is readily effected. The replacement of one H in the benzole ring increases its reactive ability and convulsive action, decreasing with an increase in number, but toxic action in another direction increases accordingly, from phenol (C_6H_5OH) to resorcinol ($C_6H_4(OH)_2$1·3.) to phloroglucin ($C_6H_3(OH)_3$1·3·5), chronic convulsions result through action upon the spinal cord. Toxicity and

physiologic action depend largely upon the relative position of the replacing groups.

In general, substitution lessens the toxic characters of phenols, provided the entering groups are not toxic—for example, salicylic acid, gallic acid, sulfocarbolic acid.

The hydroxyl group is intimately associated with the toxic action of morphin, which, through its *narcotic* characters, differs from all other opium alkaloids, its action being chiefly upon the *nerve centers* of the brain. Upon closing these OH groups through the replacement of one or both of the hydrogens by alkyl or acid radicals, the narcotic characters disappear, where, on the other hand, a *spinal excitant* (tetanic action) is developed, increasing with the number of alkyl radicals introduced. Thus codein produces like morphin (but in lesser degree) narcosis followed by an elevated reflex excitability which, if the dose is sufficiently large, develops tetanic convulsions. Dionin (ethyl ether of morphin) is more active than codein. Other members of this class are Peronin (benzyl morphin) and Heroin (di-acetyl morphin). These substances, while less active for relieving pain, exert a sedative effect on the unstriped muscles of the bronchi and reduce the disposition to cough, hence are of value in phthisis, bronchitis, asthma, etc.

Morphin $C_{17}H_{17}\begin{cases}OH\\NO\,.\,OH\end{cases}$

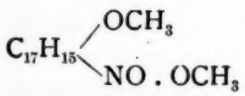
Codein $C_{17}H_{17}\begin{cases}OH\\NO\,.\,OCH_3\end{cases}$ *Methyl morphin.*

Dionin $C_{17}H_{17}\begin{cases}OH\\NO\,.\,OC_2H_5\end{cases}$ *Ethyl morphin.*

Peronin $C_{17}H_{17}\begin{cases}OH\\NO\,.\,OC_6H_5CH_2\end{cases}$ *Benzyl morphin.*

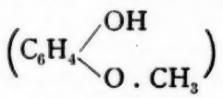
Heroin $C_{17}H_{17}\begin{cases}O-CH_3CO\\NO\,.\,O-CH_3CO\end{cases}$ *Di-acetyl-morphin.*

The most toxic alkaloid of opium is Thebaïn, which, according to Stockmann, aside from its narcotic action in small doses, is identical in tetanic effect to strychnin.



Thebaïn.

Pyrocatechol ($C_6H_4(OH)_2$ 1.2.) through conversion into guaiacol



develops an irritating action on the spinal cord.

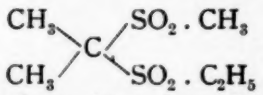
Observations prove that it is not the hydroxyl groups in themselves nor always the terminal groups that determine solely the action of a substance, but the character and complexity of the molecule. However, these groups assist in bringing the entire molecule into action with certain chemical compounds in the organism. When the reactive group which exerts the selective action of the compound in the organism is slightly altered or covered, then under conditions we can prevent the action of the entire compound. Between such terminal groups as hydroxyl or methoxyl and certain nerve centers or points in the organism where chemical substances react, definite chemical relations must exist. Through changes in these terminal groups we are able to move the point of attack of the substance or to render it absolutely inactive, but as long as it remains active, the fundamental characters of its action (although frequently modified) always manifest themselves, as for example the alkaloids and their derivatives.

INTRODUCTION OF ALKYL RESTS.

The replacement of a hydroxyl by an alkyl rest renders the entire body chemically and pharmacologically more resistant to oxidation in the system. Alkyl groups, more especially the ethyl, impart a narcotic effect. This narcotic and analgesic action is independent of the chemical character of the substance, it being a specific property of this group alone. The methyl group exerts a like effect, but much weaker and less certain. Higher alkyl rests present no advantages over the ethyl. Thus, through the introduction of an oxyethyl group into caffeine (ethoxycaffeine) an additional narcotic action is developed.

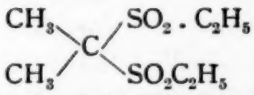
Disulfones which contain ethyl (— C_2H_5) groups are active, and the intensity of effect evidently depends upon the number of such groupings contained in the molecule.

A disulfone containing but one ethyl group



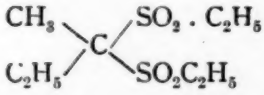
Ethyl-methyl-sulfone-di-methyl-methane

produces an effect only half as intense as that of one containing two such groups as sulfonal,



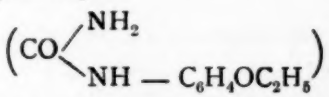
Diethyl-sulfone-di-methyl-methane.

Again, sulfonal is less active than trional, containing three ethyl groups.



Diethyl sulfone-methyl ethyl-methane.

Tetronal $(C_2H_5)_2C(SO_2C_2H_5)_2$ containing four ethyl groups is more markedly sedative than hypnotic. An interesting fact is that para-phenetol carbamid (Dulcin)



is sweet, while the methyl derivative is tasteless. The ethyl group has a certain fixed relationship to the nervous system, as shown by most bodies containing the ethyl radical. Ehrlich has found that ethylated colors stain the nerve cells, while those containing methyl groups failed.

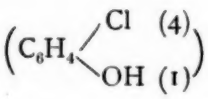
CHLORIN.

In general the introduction of chlorin in aliphatic compounds produces bodies of a more or less narcotic action where active antiseptics result if the substituted body belongs to the aromatic series. Too extensive a substitution will develop unpleasant caustic action. The introduction of bromin does not yield compounds of any greater antiseptic value than those produced by iodin.

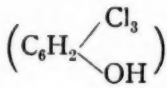
Iodin imparts to all bodies of both series strong antiseptic properties, promoting resorbtion and granulation. The substituted

iodin should be in a sufficient unstable condition so that under influence of the secretions it will be slowly liberated.

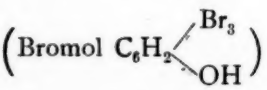
The toxic effect of aliphatic chlorinated products stands in direct ratio to their narcotic action; the more chlorine introduced the greater the toxicity, when otherwise no change in stability and physical relationship has occurred. Thus methylene chlorid (CH_2Cl_2) is less toxic than chloroform ($CHCl_3$) and is a lighter anæsthetic. On the other hand, tetra chlor methane (CCl_4) is far more dangerous than chloroform. The simpler aldehydes, as formaldehyde (HCHO) or acetaldehyde (CH_3CHO) are of an irritating nature. This character disappears upon the introduction of chlorin, attaining a maximum hypnotic effect in the tri chlor-substitution product (chloral CCl_3CHO). The antiseptic effect of the benzole derivatives increases with addition of halogens; thus para-chlorophenol



trichloro-phenol

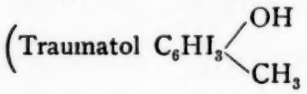


and tri bromo-phenol

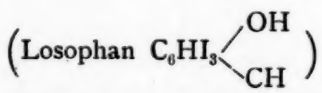


are all active antiseptics, the latter being the most active.

The iodin substitution products play a still more important part among the antiseptics, as, for example iodoform (CHI_3), iodo cresol



tri-iodo-cresol

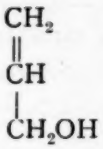


Aristol (di-thymol-di-iodid), Europhan (iso-butyl-cresol-iodid $(C_6H_3(C_4H_9)CH_3O)_2HI$).

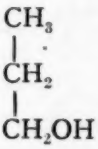
DOUBLE LINKAGE.

According to Loew, "bodies with double linkage are more toxic than the corresponding saturated ones."

For example, Dr. Miessner has shown that those engaged in the preparation of allyl alcohol



suffer serious toxic symptoms, while the corresponding saturated propyl alcohol



is non toxic.

The trebly linked di-iodo-acetyliden

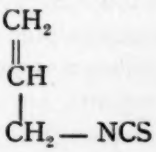
is an energetic poison, likewise allylamin ($CH_2 = CH - CH_2 NH_2$) also vinylamin ($CH_2 = CH . NH_2$).

The same influence is noticeable in the non-toxic singly linked alkyl groups of cholin as compared to the very toxic doubly linked in neurin.

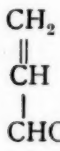
Cholin $(CH_3)_3N\begin{matrix}CH_2 - CH_2OH \\ OH\end{matrix}$ *Tri-methyl-oxy-ethyl ammon-hydroxid*

Neurin $(CH_3)_3N\begin{matrix}CH = CH_2 \\ OH\end{matrix}$ *Tri-methyl-vinyl-ammon-hydroxid.*

Allyl mustard oil



acrolein



and crotonic aldehyde ($CH_3 - CH = CH - CHO$) are all more toxic than the corresponding saturated groups.

(*To be continued.*)

THE STORY OF THE PAPAW.

By F. B. Kilmer.

"The slim papaya ripens its yellow fruit for thee."—*Bryant.*

Grant Allen tells us that no plant can be properly understood apart from its native place. Therefore, we begin our study of the *Carica Papaya* in its tropical home.

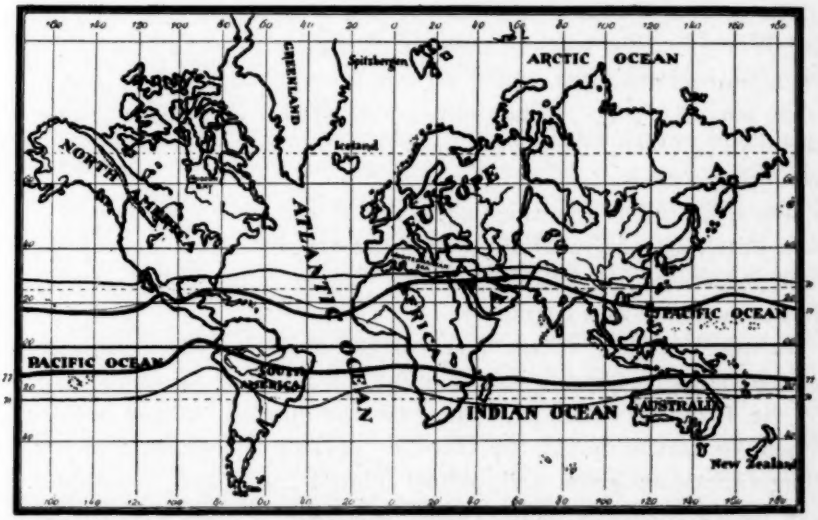
The *Carica Papaya* is accredited as indigenous in Central America. Observations and correspondence lead me to conclude that it has become acclimated in the hot regions of three continents. The zone of most abundant growth seems to lie between the isothermal lines of 77°, wherever soil and rainfall are favorable. It is grown by cultivation north and south of these lines. (The papaw is seen as far north as Jacksonville, Fla., and in Southern California.)

In these tropical lands, where every tree or plant has its peculiar legends and myths, the views of the natives upon plant life are considered unscientific and valueless, but I have found that, when stripped of the terms of superstition, some of their observations, compared with our scientific knowledge, are not far apart. Their apparent veneration for trees and plants is based upon intimate association, wherein they have come to a knowledge that plants eat, drink, marry, propagate, care for their offspring and bestow blessings or curses upon all living things, including man. This is about all that anybody can know about them.

Many trees are famous in these lands, none more so than the papaw. Conflicting stories as to its powers and properties are due somewhat largely to the fact that different species, or variations in species possessing varying characteristics, are found in these localities.

Quite universal is the knowledge of the unique property that has given to this tree its world-wide fame, viz.: the power of its milky

juice to soften and dissolve tough meat. The statement has passed current in our journals that the emanations from this tree will dissolve and digest albumin, and that it is the custom of natives to hang meat and chickens in the branches of a tree to render them tender and edible. The natives often go farther than this; they state that if male animals browse under the papaw tree, they thereby become emasculated. If we compare this statement with the alleged property of the roots as a generative tonic, we shall have a marvellous combination of an aphrodisiac and an anaphrodisiac in the same plant.



The Carica Papaya grows prolifically between isothermal lines of 77°; is grown by cultivation between the lines of 70°.

It is needless to urge that such stories are exaggerations of the pepsin-like properties of the fruit.

The native uses of the papaw are numerous and varied. The bark is used in the manufacture of ropes; the fruit is edible, and, according to local conditions, may be sweet, refreshing and agreeable, or in other localities it is sickly, sweet and insipid. The fruits find a large consumption by the natives, and are considered very nutritious.

At the corner of a sugar-cane field where the ragged canes bend over in a wild green, brown and yellow tangle, there will be stand-

ing a papaw tree, and if the time of the papaw has quite come, beneath the tree will be assembled a half dozen negroes.

The ripe fruit is eaten as we eat melons. Salt enhances the flavor, and some users add sugar. The melons must be perfectly ripe when eaten raw, as the green fruit contains a strongly marked acrid principle. The color of the ripe fruit is more or less that of our very yellow muskmelon. The sweetness of its resinous, pulpy juice clings to the tongue and remains prevalent for some hours.

The natives enjoy the flavor, while the stranger has to acquire the liking. Excellent preserves are made of the ripe fruit, which, for this purpose, is boiled down in sugar and candied (like citron).

At the sugarhouses slices of the papaw are often seen seething in hot syrup. The slices of melon combined with some acid fruit is made into native tarts, which articles correspond more or less to what we call "pies." The fruit is also stewed and served on the table. The green fruit is made into plain and spiced pickles, which are highly esteemed.

The fruit, just before ripening, is peeled and sliced, macerated in cold water, with frequent changes of the water for some hours; the then macerated fruit is dropped into boiling water, boiled sharply and then served as a vegetable.

In every tropical village one will find a market place set apart where the native products are bought and sold, and in such a place by the roadside, under the shade, are the market women in their quaint baskets or bowls, the traveller finds an astonishing and puzzling variety of green and yellow colored fruits and vegetables. The papaw is always there in abundance, and a most frequent cry of the sellers is, "Aqui estan las Mameo," or "Ca qui ulè papayá ca qui ule."

As an article of food one finds the papaw prepared in a score of ways, making a variety of edible dishes, which, from the native standpoint, would be expressed in our language as "wondrous and nutritious delicacies."

A plant so universally distributed and possessed with such varied properties, naturally takes an important place in the native materia medica. In the native parlance, "It makes him much well."

The seeds are reputed as anthelmintic[1] and emmenagogue; they are also used as a thirst quencher, form component parts of a drink used in fevers, as well as being used as a carminative. Syrups,

wines and elixirs made from the ripe fruit are expectorant, sedative and tonic.

A malady which the natives call the "cocoa bag," is a troublesome tropical disease, reputed to be hereditary and contagious; at all events, it seems to lurk in the blood of persons of otherwise apparently good health and habits. Suddenly the victim becomes a mass of offensive sores, debilitated, etc. The native doctors add the papaw fruit to the diet drinks used in this disease, and succeed in moderating its violence, at least. To the sores a paste made with the papaw milk as one of the constituents is also applied.

The slight pimples accompanying the first stages of the yaws soon spread into ulcerous sores that cover the entire body. Here, too, the claim is made that a slice of the papaw rubbed over the pimples will abort them. It is also claimed that the ulcers may be cleaned in a similar fashion.

I witnessed a most striking cleansing of a black foot in which the chiga had bored and laid its eggs, producing a mass of foulness beyond description. Here a paste of the papaw milk was pushed into the seething mass and kept there for forty-eight hours. It was then flushed, curetted, and antiseptics were applied. A clean wound which readily healed, resulted.

The green leaves or slices of the green fruit of the papaw are rubbed over soiled and spotted clothes, and by its power of dissolving stains, papaw has acquired the name of "melon bleach." The leaves or a portion of the fruit are steeped in water and the treated water is used in washing colored clothing, especially black, the colors are cleaned up and held fast.

The seeds are eaten as a delicacy. They have quite an agreeable taste, something on the order of the water-cress and a piquancy slightly suggestive of the mustard family. Macerated in vinegar they are served as a condiment.[2]

The strange and beautiful races of the Antilles astonish the eyes of the traveller who sees them for the first time. It has been said that they have taken their black, brown and olive and yellow skin tints

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[1] The anthelmintic properties residing in both the seed and juice have been noted by various authorities.

[2] The seeds are encased in a slimy coating and advantage is taken of this by the younger generation, who spread them out on a board, and by this means form a "slide," which corresponds with the frozen gutters so agreeable to our northern urchins.

from the satiny and bright hued rinds of the fruits which surround them. If they are to be believed, the mystery of their clear, clean complexion and exquisite pulp-like flesh arises from the use of the papaw fruit as a cosmetic. A slice of the ripe fruit is rubbed over the skin and is said to dissolve spare flesh and remove every blemish. It is a toilet requisite in use by the young and old, producing, according to the words of a French writer, "the most beautiful specimens of the human race."

The papaw has been brought to America as a cure for the national disease, dyspepsia. In its tropical home there are no dyspeptics, but its use along similar lines is by no means unknown.

The meat in these countries is tough and tasteless; beef, mutton, pork or fowl have the same flavor, and are as tough as hickory wood; boiling until they fall to pieces does not render them any more edible; they simply change from solid wood to fine tough splinters.

One reason for this is that in this climate meat must be eaten immediately after slaughter. (It often reaches the pot in an hour after killing.) The papaw helps to overcome this Rubbed over tough meat it will render it soft and change a piece of apparent leather to a tender, juicy steak. It is put into the pot with meat, enters into the cereals, soups, stews and other dishes, and they are made at least more edible and digestible.

Most of the half-breeds of Indian extraction upon the South American Continent and adjacent islands are particularly given to meat diet; many of them eat it raw,[3] sometimes in a state of partial decay, and here the papaw is brought into use, being eaten with the flesh or rubbed over it before it is eaten.

Some of these people are great gluttons; they gorge themselves until the skin on their distended stomach is stretched to its utmost. It is certain that no human being could digest the kind of food and the enormous amounts they consume without the kindly aid of the papaw fruit to assist digestion.

NAMES AND CHARACTERISTICS.

The botanical characteristics of this family having been more or less completely described by various authors, need not here be

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[3] In Bolivia and Paraguay it is a very common sight at the railway stations to see raw meat peddled out in chunks to passengers.

repeated. Of the many species the following are edible: *Carica cauliflora, C. pyriformis, C. microcarpa, C. integrifolia, C. Papaya* and *C. quercifolia.*

The *Carica digitata* is credited with poisonous emanations, and its juice is actively poisonous, causing pustulation when applied to the flesh.

The *Carica Papaya* is designated by different names in the various localities where found. For instance, in Mexico, "lechoso," in Brazil, "papai," "maneo" and "mamerio"; in Paraguay, "mamon."[4]

Here, too, the term "jacarata" (chakarateca) is applied to the *Carica Papaya*, as well as to several trees of the same natural order. In Yucatan the native uncultivated variety is designated as "chich put," or little papaya, while the cultivated is simply "put." The Spaniards designated the original species as "papaya los pajaros" or "bird papaya." The term "papaw," though sometimes applied to several species, almost universally means the Carica Papaya.

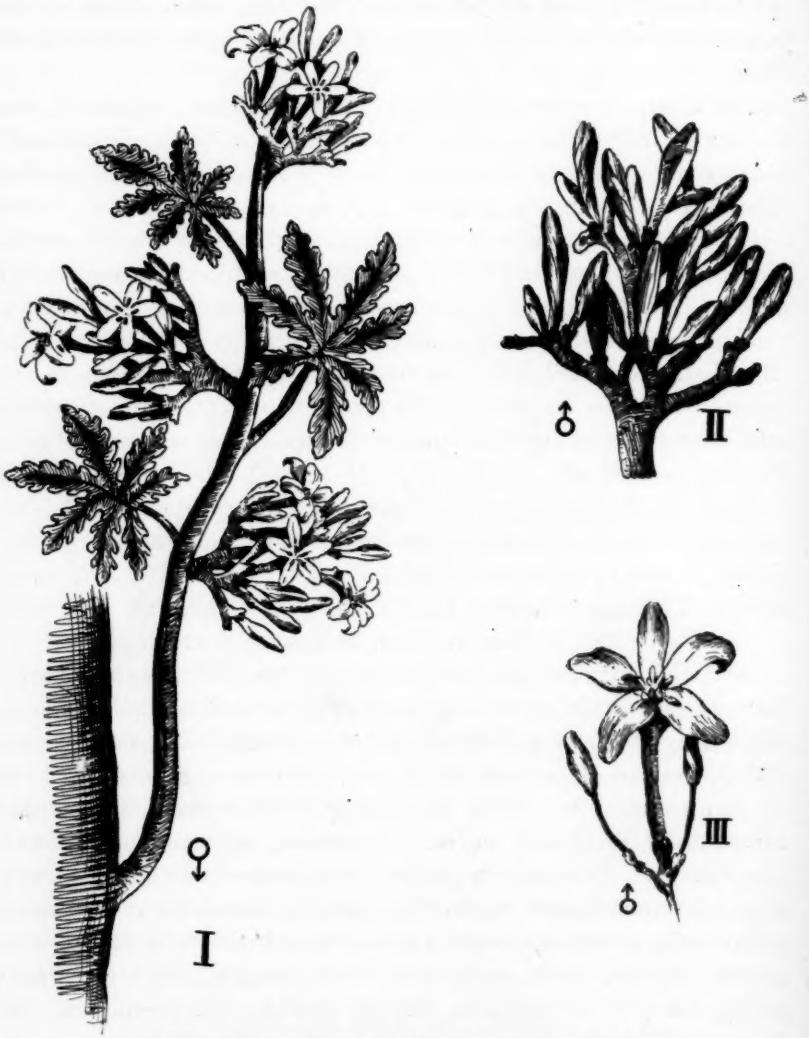
Among the names by which botanists have designated this plant are the following: Papaya fructu melopeponis, Tuournefort; Papaya Carica, Gaertn; P. lyatira, Tuss; P. vulgaris, A. D. C.; P. Orientales Col.; Carica Papaya, L.; C. Maniaya, Vell.

The *Carica Papaya* may, in brief, be described as follows:

A single, supple, slim, straight stalk, terminating in a group of large leaves which are arranged in the form of an umbrella, branching only when its growth is interfered with. Cultivated plants attain a height of from 10 to 30 feet; wild varieties push up to 60 or even to 100 feet. Near the base of mature trees the diameter ranges from 6 inches to 1 foot. In a young plant the stalks consist of a cellular pith filled with water; in a mature tree that portion of the trunk immediately under the bark is fibrous for a few inches, followed by a soft inner layer of an inch or more, terminating in the central portion, which is hollow. At intervals through the hollow centre are seen membranous tissues dividing the cavities into sections, and in the rainy season, for a considerable height up the trunk, this central cavity is filled with water. The wood of the

[4] In Brazil the uncultivated plant is designated as "mameo-femeo"; the cultivated form of the same as "mameo-meleo;" the hermaphrodite plant "meneco-macho."—(Rusby.)

papaw is soft, white and spongy; cuts easier than a potato; is full of water, decays rapidly, and is not useful for any purpose. The trunk is covered with a gray (green at the top) smooth, tough bark



I.—Carica Papaya, branch of Male or Hanging Papaw.
II.—Staminate flower.
III.—Male flower.

laid on in folds, which at intervals form rings.

A large turnip-shaped tap-root reaches down to seek nourishment

and to give stability to the tree. These roots are similar in structure to the trunk, except for a white bark, and possess an odor of cabbage and a peculiar taste suggesting radishes. The leaf stems are large and hollow, cylindrical toward the leaf and flattened at the point where they join with the stalk. The leaves are large palm-lobed, with somewhat deep indentations, dark green on the upper and light green on the under side. They are short-lived and, as the tree shoots upward, they drop off, leaving scarry marks in the bark of the tree trunk.

The locality where grown, as well as the effects of cultivation, modify the character of this plant, hence we find on record varying

IV.—Pistillate flower.
V.—Young fruit.
VI.—Seed seen in section.

descriptions and statements. Among the notable varieties of the Carica Papaya are the green and violet. The latter species which has had considerable attention paid to it, is the one most highly esteemed for cultivation, but does not attain great height. The stalk and limb portion of the leaves are violet color. The fruit is large, often weighing as high as twenty pounds, and when ripe is very sweet. While young the trees are kept shady, and pruned to prevent their growing tall. To encourage fruit, portions of the flowers are picked off; the smaller fruits are removed when green, so that the remainder will grow larger and stronger. By cultivation a dwarfed variety ("lechoso enana") is produced. The green Carica grows to greater height than the purple; its fruits are smaller and possess a less agreeable flavor.

The three forms of flower present in the papaw are, according to

the native description, classified as varieties. The so-called female trees bear only fruiting flowers and produce the largest fruit and the greatest numbers. These flowers are single, with a yellow (or purple) corolla with five sessile petals, growing in considerable numbers at the apex of the stalk, which rapidly pushes upward and puts out new leaf stems. The fruit development is so rapid that buds, flowers, green and ripe fruit are often seen at the same time. The male flowers are borne on hanging stems, ranging from 6 inches to 1 foot or more in length (hence the "hanging papaw"), and may be white, bright yellow, sometimes tinged with purple, often developing considerable fragrance. The hanging stems in older trees bear fruiting flowers and present a somewhat curious sight. The fruit of the hanging papaw is not large, but is very sweet. The fruits vary considerably in form as well as in size. They are orange shaped, squash-like or quite resembling the cocoa pod; again, they resemble muskmelons, and in the highly cultivated variety watermelon shapes are seen. The fruits are green (or purplish cast) turning yellow when ripe.

The skin of the melon is smooth and thin. Before ripening the greater bulk of the latex lies just under this skin. The flesh of the green fruit is white, tough and watery. As the fruit ripens it turns to a muskmelon yellow, with a thickness of about 1½ inches, ending in a central cavity which is filled with seeds attached to and held together with a delicate membrane, which constitutes the inner skin of the fruit.

The seeds when fresh are dark brown, changing to black on drying. Before desiccation their outer membranous coating is transparent and slippery; the inner coating is hard, horny and wrinkled, and between these two coatings lies a mucilaginous substance containing myrosin. Within the inner shell lies the leaf-like cotyledons, veined at the base with an albuminous homotropal embryo with a roundish radicle easily distinguished when slightly magnified.

The seeds when dried resemble pepper. They are aromatic, pungent, piquant but not as sharp as mustard, their taste slightly suggesting water-cress.

CULTIVATION AND GROWTH.

It is quite common for numerous papaw plants to spring up from seeds scattered by the birds over a portion of land which, accord-

ing to tropical custom, has been cleared by burning away the trees and undergrowth. There are no forests of papaws because the plants need sun and room. They are seldom seen among dense growths. They do not progagate in clusters. For the most part they are the product of cultivation, and near every hut are carefully guarded groups from two to six in number.[5]

They present a striking appearance with their straight slim, shiny stalk; their bright green umbrella tops towering above a

"Hanging Papaw."

wilderness of flower-sprinkled verdure. Most beautiful specimens are seen in such a place, their base covered with a tangled undergrowth of trailing, climbing vines. Their roots are kept moist by fallen leaves; and enriched by nuts and fruits that fall and rot among the masses of forage and litter so abundant in tropical gardens.

[5] This has particular reference to the habits of the *Carica Papaya*. Certain varieties such as the *Carica quercifolia*, *C. microcarpa*, etc., are sometimes found in the dense forests.

The only cultivation they can possibly receive must come from a little house waste promiscuously thrown from the hut, the browsing of the ever present dogs, asses and goats. But under these conditions fruiting is generally abundant. They exhibit somewhat the characteristics of the melon tribe. The young plants are exceedingly sensitive and tender; under slight adverse conditions they succumb and die.[6]

A place where it never rains but always pours seems best suited to the papaw. My records show the most thrifty trees in spots where it rains nearly every day in the year; pouring, soaking rains with a fierce, bright sun shining all through the downpour. After the rain come the insects, lizards, centipedes and other creeping things that delve among the roots and climb up the stalk of the papaw and do the real cultivation. The plant will not flourish in swampy nor sandy soil, and seems to be at its best in the rich humus of the hillside.[7]

It grows at the edge of the sea with the waves washing the roots, luxuriates in the high mountain plateaus in all of the windward and leeward islands; it flourishes but does not attain to any great

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[6] Professor Rusby ("Carica Papaya," *Druggists' Bulletin*) has stated that this tree "can be propagated and grown with great readiness; that its vitality is so great that it is with difficulty destroyed until its natural course has been run." Six years' observation has convinced me that it is exceedingly difficult of cultivation, and that the cultivated trees are most easily destroyed by adverse conditions.

[7] The following is an incomplete analysis of a plot in Jamaica on which were several fine specimens of the papaw:

Water (in air-dry sample)	5·02
Volatile matter	20·12
Silica	32·72
Lime (as oxide)	10·62
Magnesia (oxide)	1·00
Potash (oxide)	·52
Sodium, trace	
Magnesia, trace	
Aluminum (and iron)	8·64
Carbonates $(CO)_2$	5·81
Phosphoric acid	10·20
Sulphates, trace	

[8] In Venezuela thrifty specimens are cultivated in the sandy soil of the ravines. There is here, however, a rainfall averaging one metre per annum and the climate is very equable.

height, on the bare coral rocks of Yucatan. In parts of Peru it grows prolifically without much cultivation or care, and it is reported that in the Transandine regions it reaches a height of over one hundred feet.

In some localities the plant begins to grow fruit in seven months; in others, eighteen to twenty months from the seed. Usually its life is rather short, two to three years being the maximum fruit-bearing period. (A rare specimen was observed which was eighteen years old, and was bearing one to two fruits each year.) The fruiting of the papaw is abundant. From two to three hundred have been gathered in a season from a wild tree, in size varying from an inch in diameter to that of a baseball. The cultivated plants yield from twelve to sixty fruits, weighing from five to twenty pounds each.[9]

It is reported that in Brazil, in the French Colonies, in Algiers, and in the Island of Reunion, successful and extensive cultivations have been carried on. In the island of Montserrat a large acreage under cultivation was some three years ago destroyed by a tornado. In the island of Jamaica, under government patronage and the immediate direction of William Fawcett, director of the botanical gardens, several attempts at the cultivation of this plant were undertaken on a large scale, but the results were not encouraging. Plots consisting of five acres in the first instance and ten acres in the second were prepared by clearing, seeds were carefully selected, one portion of the seed being sown directly in the ground, other portions sown in bamboo pots, and the young plants transplanted. In the first instance, a rather fair proportion of the trees came to maturity and began fruiting, but at this stage disease set in, insects attacked the plants and the whole field was exterminated. The wild plants do not seem to be attacked by disease except after injury, but the

[9] The best method of planting papaws is to raise the young plants in beds and as soon as they are three inches high transplant them into bamboo joints, in which they can be kept until they are 9 inches high, when they can be transplanted to the open ground. In dry districts they will require abundant watering, irrigation twice or thrice a week being absolutely necessary. In wet places they can be grown with little or no water. Papaws require good, rich, deep soil and good cultivation; even then, many of the plants, just as they should commence to bear, suddenly fail, the plants cease to grow, the young leaves turn yellow and fall off.—(Wm. Fawcett, Bulletin Botanical Department, Jamaica.)

cultivated plants seem very susceptible to every sort of malady. Insects attack the tender leaves of the young plants and they wither. Fungi and bacteria find here a suitable soil.

After fruiting, and especially if the fruits are bled, the tree will take on a general debility and become the prey of every adverse circumstance. One large field was entirely eradicated by a disease or diseases which the natives attributed to attacks of the "mackacka worm."[10] In my opinion, the trouble arose from the inherent weakness of the cultivated plant in its altered environment, which rendered it susceptible to attacks of beetles and insects of various kinds.

In another series of plantings conducted with still more careful preparation of the ground and selection of seeds, coupled with care for the young plants, there was a record of a small proportion of plants coming to maturity, and of these only a meagre part bore fruit. None of the plants or their fruits were as large as those of the parent stock. All of these efforts were accompanied by phases which were puzzling and embarrassing.

The variations in plant life which one sees and hears of in these regions are somewhat interesting. It is stated that the shaddock contains thirty-two seeds, only two of which will produce shaddocks; the remaining thirty will yield sweet oranges, bitter oranges, forbidden fruit, good oranges and bad oranges, and until the trees are in full bearing no one can guess what the harvest will be. The seeds of the mango selected from the finest fruit and cultivated with care, will rarely produce anything approaching the parent stock. In fact, no two trees of the mango seem to resemble each other. The papaw is likewise very prone to variation. Seeds selected with extreme care from flourishing trees, the fruit of which would weigh fifteen pounds, upon being planted would in part follow the parent stock; other portions would revert to the wild prototype and yield fruit the size of a hen's egg.

In some of the fruits of the papaw the seeds number five, in others prodigal nature supplies over five hundred, apparently only a few of these seeds are fertile. When a native desires a single

[10] The term "mackacka worm" in the tropics is applied to the larvæ of various beetles which feed upon plants that are undergoing decay. I suppose that plants already diseased were the only ones affected, and that the ravages of these larvæ hastened decay. At the present writing these larvæ are reported as doing great injury to the logwood trees.

tree, he buries two or three such fruits in the ground, and at most two or three plants are the result. After continued experiment it was found that seeds taken from the central portion of the largest and finest fruits were the most likely to be fertile, and would give more encouraging results. The proper adjustment of the sexes in tropical soil is difficult and exasperating.

The papaw is much like the nutmeg in its vagaries of sex relation. It is generally agreed that for fertilization one male to ten female plants is the proper ratio, but until the trees arrive at the blossoming stage (five years in the case of the nutmeg) the male cannot be distinguished from the female. One can imagine the dismay of the cultivator who finds at the end of all his toil and waiting that he has a plantation of male non-fruit-bearing instead of the coveted female, or fruit-bearing plants. I have records of numerous instances where acres of ground were planted with thousands of papaw plants in which the males were in the majority of over fifteen to one.

This constantly recurring disproportion of the sexes suggests that in cultivation we were so changing environment as to cause a perversion of the sexes, resulting in a race of non-fruit bearers.

Methods of artificial fertilization and budding, such as is followed in the propagation of melons and oranges, are now in the experimental stage.

(*To be continued.*)

A FEW NOTES ON THE USE OF WOOD ALCOHOL PHARMACEUTICALLY.

By Frederick T. Gordon, Pharmacist U. S. N.

The point has been raised that one of the objectionable features in the use of wood alcohol pharmaceutically is its strong and peculiar odor, an odor that is unpleasant to many persons and which at once makes the substitution of this for grain alcohol apparent. That this is a drawback is undeniable; therefore the question has been asked if there is anything that can counteract or improve this odor. This is perfectly legitimate to answer, for there are many preparations in which purified wood alcohol can be used, *e. g.* liniments, lotions, toilet preparations, etc., without impropriety, provided that the use thereof is made known to those whom it will most concern,

the druggists, and a reasonable reduction in price is made. Any effort to prepare a wood alcohol that can be used surreptitiously in place of grain alcohol should be sternly frowned down; if it is to be used—and I hope to see it in its proper place among pharmaceutical solvents—this use must be open and above board, sanctioned by the weight of authority unimpeachable.

As far as I have been able to learn from study of the literature on the subject as found in our drug journals, there is but one way to get rid of the peculiar odor of wood alcohol and that is to eliminate the impurities that give it this odor. The addition of many essential oils and substances possessing a powerful odor will, to some extent, mask the odor of wood alcohol, but they will not mask it so that the trained nose cannot detect it, and, from some experiments I have made, I would say in addition that it is a waste of these oils even to try to hide that peculiar "methylated" odor; it will come out. The odor of wood alcohol is not due to the methyl alcohol it contains, but is due to its impurities—acetone, furfurol, methyl acetate, allyl and amyl alcohols, aldehyde, etc.—and when these are thoroughly removed we get a spirit that can scarce be distinguished from a pure grain spirit, one admirably adapted for use in making the cheaper perfumes. The process of removal is mainly chemical treatment and fractional distillation; it is profitable only on a large scale. Such a "pure" wood alcohol, or, as it is then better named, pure methyl alcohol, can now be easily obtained.

In making a number of solid extracts of some of the narcotic drugs with methyl alcohol, in which the menstruum was strong in alcohol, I made the observation that such solid extracts seemed to be more brittle and easier to powder than when made with grain alcohol, and it also seemed to me that these extracts were freer from inert extractive than the latter. This is a point that invites further investigation, especially so as it has been proven that methyl alcohol will extract the active principle of these drugs equally as well as does grain alcohol. In my work, such extracts assayed well up in alkaloidal strength, and proved easier of assay, too, from being freer from extractive matter.

Wood alcohol has been suggested for making tincture of iodine—this should be positively prohibited, as such a tincture is violently irritating, decidedly caustic in effect and will blister or cause an eruption on tender skins. When used around the face or neck, its

vapor causes great irritation of the eyes and nose—almost unbearable, and also makes the exposed skin smart and tingle. Even pure methyl alcohol tincture will cause irritation of the nose if its vapor is inhaled, an irritation quite different from that of iodine. During the winter I made a number of experiments on wood alcohol tincture iodine, having a number of cases under my observation where the chest was painted with iodine for simple cough and cold, painting one side of the chest with wood alcohol tincture, the other with grain alcohol tincture. In every case the difference was marked, the wood alcohol side appeared much redder the second day, there was sometimes faint blistering, and the patients declared that this side "burnt" them the most. In applying this there was often caused very unpleasant symptoms from the irritating effect of the vapor on the eyes and nose, one case of mild conjuctivitis being noted. In a severe case a blistering effect was wanted; this was obtained easily by painting the wood alcohol tincture on thickly and covering it with a piece of oiled muslin. The burning pain became so great in ten or fifteen minutes that the muslin had to be taken off and vaseline applied. From this experience I would say that the wood alcohol tincture of iodine is only fitted for veterinary practice, or for cases in which strong irritating effects are called for, and I might add that in general the effects of this tincture were distinctively less satisfactory in my cases than the U.S.P. tincture.

Noting that the peculiar irritating effects seemed to come from the vapor of the wood alcohol tincture, I sought the reason for this, and I think it lies in the formaldehyde and formic acid formed in this tincture by the action of iodine on wood alcohol, or some of its impurities; for the tincture made with pure methyl alcohol yielded much less pronounced results. One hundred c.c. of tincture were made, U.S.P. strength, and allowed to stand ten days, to get as much action by the iodine as possible; this was then distilled in fractions of 10 c.c. and each of these examined. The distillation began at 66° C., running up to 68° for the last four fractions. The first fraction was of a light straw color, contained a trace of iodine, reduced silver solutions at once and gave marked reactions for formaldehyde and formic acid. To make sure of the former, a number of tests were applied to the distillate—all gave very positive reactions. I did not then estimate the amount of formaldehyde formed from given quantities of each of the substances, but this I

hope to do soon, as I have a tincture I am keeping for several months, distilling off fractions monthly. The first four of the fractions contained practically all of the formaldehyde and formic acid; the amount of iodine in each increased progressively, the last two fractions being very dark in color, the tenth fraction not being distilled over.

A curious behavior of the first two fractions seems worthy of mention. As I remarked, these were light straw color No. 1, and pale yellow, No. 2; when exposed to the direct rays of the sun in tightly corked vials they became colorless in an hour or so; left standing uncorked over night, the color returned. This experiment was repeated several times, the color gradually fading until now, a couple of months later, the two samples are water-white and do not react for free iodine. Both still give the formaldehyde reaction p ainly.

Another point. Although there is a small difference in the specific gravities of wood and grain alcohol, the two tinctures I made had practically the same specific gravity, the difference in the appearance of the two tinctures would lead one to think that there is at least ten or fifteen points between them. The wood alcohol tincture seemed very thin—" watery " is a term that somewhat describes it—and has very little " body," it is more limpid and spreads on the skin with great rapidity. Its color, too, is different; it has more of a greenish-yellow tint in thin layers than the mahogany brown of the grain alcohol tincture, and is more transparent. One who has seen both tinctures could readily detect the wood alcohol tincture by its general appearance alone. However, if a pure methyl alcohol is used, there is very little difference between it and the U.S.P. tincture in general appearance; neither is it much more irritating, either to the skin or in its vapor. No doubt the great difference is due to the many impurities mentioned as being present in wood alcohol. Referring back to specific gravities, the specific gravity of my wood alcohol tincture iodine was 0·877 to 0·875 for grain alcohol tincture.

Pure methyl alcohol seems to be well adapted for the making of resins from crude drugs; its lesser cost would be a great advantage to the pharmacist if its use were made permissible. I made a few experiments in this line with podophyllin and jalap, and would report that I got results every bit as good in yield, appearance

and activity from methyl alcohol as I did with grain alcohol in a series of parallel exhaustions; indeed, the resins so obtained could not be told from one another. In fact, I think the question of permitting the use of *pure* methyl alcohol for such operations, the making of solid extracts and similar preparations in which the solvent is completely removed from the finished article, to be well worthy of thought and study by our Pharmacopœial Revision Committee, for such use would greatly cheapen the cost of many drugs without impairing their efficiency at all.

METHYL ALCOHOL IN PHARMACEUTICAL PREPARATIONS.

By E. Fullerton Cook.

The question recently raised concerning the justifiable use of methyl alcohol in preparations for internal or external use has been prominently brought before the manufacturer and pharmacist and it is desirable that some conclusion be reached.

At the request of Professor Kraemer some of the more recently published journals, those of 1901, have been reviewed for reports in favor or disfavor of its use, and abstracts are submitted from those which add to the literature on the subject.

The communication from Mr. Frederick T. Gordon, published in the *American Druggist*, of February 25, 1901, is prominent among those in favor.

In almost none of the unfavorable criticisms does there seem to be a discrimination in the use of the terms "wood alcohol" and "purified methyl alcohol," and this is unfortunate, as Mr. Gordon has said, since the commercial wood alcohol cannot, at any time, be considered a rival of ethyl alcohol in preparing pharmaceutical preparations.

We must, however, accept all evidence obtainable, and carefully determine its value, and with that end in view the following are presented:

Dr. A. G. Thompson (*Pharmaceutical Review*, Feb., 1901, 51), as early as 1897, reports an instance which came under his observation, of complete blindness caused by the drinking of an essence of ginger.

During 1898–1899, Kuhnt, MacCoy and Michael, Moulton, Holden, Gifford, Patillo, Callan and others report cases of blindness from the drinking of "methyl alcohol."

In February, 1899, Hiram Wood reports in the *Ophthalmic Record*, six cases of total blindness caused by the substitution of an essence of ginger for other alcoholic drinks.

As long ago as June, 1877, Viger published an account of a similar case in *l'Année Medicale.*

The symptoms of a typical case are as follows: about an hour after drinking severe headache, vomiting, excessive sweating, dilation of pupils and delirium.

In twenty-four hours the delirium and other symptoms have disappeared but total blindness remains.

The sight gradually improves during the next two months, but eventually permanent loss of sight results.

A large dose of wood alcohol taken upon an empty stomach has been known to cause death after several hours, while complete recovery has been reported when but a small dose was taken.

On March 6th, at Crisfield, Maryland, a man, after drinking a large quantity of an essence of ginger, was taken violently ill and, though given careful treatment in a Baltimore hospital, subsequently became entirely blind.

On April 19, 1900, a man at Circleville, West Virginia, drank some essence of peppermint and essence of lemon in lieu of whiskey or brandy. Although experiencing almost total blindness during the next few days, his sight gradually grew better.

On September 6th, at Fawn Grove, York County, Pa., the drinking of some essence of ginger resulted in the death of two men and total blindness of another.

The essences causing the trouble in these last mentioned places, Crisfield, Md., Circleville, W. Va., and Fawn Grove, Pa., were all manufactured by one firm and, samples having been obtained, they were subjected to analysis, the results being published by H. P. Hynson and H. A. Brown Dunning in the *Pharmaceutical Review* of February, 1901, p. 54.

They obtained a distillate of the samples and made comparative tests with a mixture containing 75 per cent. Columbian spirits and 25 per cent. ethylic alcohol, which led them to conclude, that the distillate was a similar mixture.

In the communication above mentioned they say: "We believe that the results secured are such as to convince almost any one that wood alcohol is present in large quantities in the essence of ginger examined. It must also be concluded, since the tincture of ginger made with ethylic alcohol has never produced the toxic and sight-destroying effects described by Dr. Harlan, that methylic alcohol is entirely unfit for internal administration."

In the *Bulletin of Pharmacy*, of March, 1901, page 96, an instance is reported of a party of four men having indulged in the drinking of some essence of ginger that resulted in the death of two, and only the most active efforts on the part of the physicians saved the other lives.

The *Druggists' Circular*, of March, 1901, reported another case in which a sailor, during "shore leave," drank a quantity of essence of ginger. He experienced the symptoms before mentioned, followed by permanent blindness.

The instance cited by Drs. MacCoy and Michael, several years ago, was that of a young man who, while convalescing from measles, succeeded in obtaining two ounces of methyl alcohol, "the article being a highly purified one." Two hours afterwards he took a similar quantity and as a result experienced the usual, immediate symptoms and eventually almost total blindness.

In the same article, in commenting upon these cases they say, "There can be no reasonable doubt that all the people mentioned above were simply poisoned by wood alcohol; as in addition to the finding of that substance in the ginger preparations, it is shown that the same result followed the use of a peppermint essence in which it was also detected." * * * Whether the wood alcohol used in making the preparations which have brought about such dire results was "crude" or "purified" is apparently unknown. It is reasonable to infer, however, that anyone employing it for such purposes would choose the latter on account of its comparative freedom from disagreeable odor. * * * The foregoing should sufficiently dispose of all theorizing as to the possible harmlessness of a purified wood alcohol. Even if it were known that it could be so purified as to render it no more harmful than grain alcohol, one would have to remember that there would always be uncertainty as to its purification having been fully accomplished. With ordinary alcohol we have no parallel risk."

In answering a query in the *Pharmaceutical Era*, April 11, 1901, page 393, "May wood alcohol be used as a preservative for witch hazel?" they say that the manufacturers of Columbian spirits state in their advertisements that it cannot be used internally.

In connection with this, the attention of all who may be interested in this subject should be called to an article published by Ferdinand A. Sieker on "The detection of methyl alcohol in pharmaceutical preparations," appearing in the *Pharmaceutical Review* of March, 1901, and other journals.

It is interesting to note that, according to Mr. J. Wolff, in a paper reported at a recent meeting of the Paris Académie, distinct traces of methyl alcohol are found in the fermented juices of many fruits, amounting to as much in some instances as two (2) volumes for every one hundred (100) of ethylic alcohol formed and in other fruits only 0·2 volumes to the same quantity of ethyl alcohol. See *Compt. rend.*, 1900, p. 1323. *Zeitschr. f. Unters. d. Nahr. u. Genuss.*, 1901, p. 391.

It will be noticed that we have no reports on the use of methyl alcohol as a menstruum in the making of such preparations as those in which the final product contains none of the solvent, although, as Mr. Gordon says, the various manufacturers could, no doubt, furnish some very interesting, possibly conclusive evidence, if they would but report their experiences; neither do we have any report upon its use in the making of toilet preparations, although one man vigorously protests against the very thought of its use in this connection. He evidently is familiar with the commercial grade only and not the "exceptionally pure and odorless article."

Likewise there is almost no mention of its use in preparations intended for external application.

In view of the facts above cited it is claimed that pharmacists at present are not justified in substituting methyl alcohol for grain alcohol when the preparation is intended for internal administration. For heating purposes it may well take the place of the more expensive liquids, also as a solvent in the preparing of solutions to be used in the arts, as varnishes, etc., and seemingly without objection in the making of pharmaceutical preparations in such cases where none of the methyl alcohol remains in the finished product.

AN INVESTIGATION OF COLCHICUM.[1]

By Louis Schulze.

Query 15.—"Colchicum root and seed both contain as their principle colchicine an alkaloid. Why should both be official, and which is preferable, and for what reasons?"

If colchicum depends upon the alkaloid colchicine for its therapeutic value, then, it seems, only that portion of the plant containing the largest amount of this alkaloid should be official, and all galenical preparations be made from that portion.

Colchicine differs from most alkaloids in the following particulars:

(1) It is removed from acid solutions by shaking with chloroform.

(2) It is quite freely soluble in water.

(3) It is precipitated by Mayer's reagent only from strongly acid solutions.

This alkaloid is, furthermore, very easily decomposed, its aqueous solutions rapidly losing strength, even when quite neutral. Mineral acids, even quite dilute, decompose it on application of heat.

In assaying the root and seed for ascertaining the percentage of colchicine three methods were pursued, namely:

First Method.—100 grammes of the powdered drug were placed in a flask, and 100 c.c. of Prollius' mixture added. After securely corking, this was macerated, with occasional shaking, for twelve hours. After decanting 50 c.c. of the clear fluid, it was evaporated on a water-bath in a beaker nearly to dryness. The residue was taken up until 10 c.c. of ether and 5 c.c. sulphuric acid (2·5 per cent.) added and stirred until the ether was evaporated. The acid fluid was then filtered into a separator, retaining the insoluble residue as much as possible in the beaker. This residue was redissolved in a little ether, and 2 c.c. of the dilute acid added, stirring as before, and filtering the acid aqueous solution into the separator. After washing the filter with a little of the acid, the washings were added to the contents of the separator and 15 c.c. of chloroform shaken carefully with it during two minutes. It was then allowed to separate and the chloroform drawn off into a tared beaker. This treatment was continued with two portions of fresh chloroform (10 c.c. being used

[1] Eighteenth Annual Proceedings of the Maryland Pharmaceutical Association, June, 1900, p. 119.

each time). The aqueous solution remaining after evaporating the chloroform was tested with Mayer's reagent, one-half strength solution being used, and in case of seed, on discovering the alkaloid had not been entirely removed, again treated with chloroform. Finally the chloroformic solutions were evaporated to dryness, redissolved in a little dilute alcohol and again dried to a constant weight. This residue was nearly pure colchicine. As it might have retained some chloroform, it was once more dissolved in dilute alcohol and dried.

Second Method.—10 c.c. of fluid extract was diluted with 85 c.c. of water, and solution of lead subacetate added in slight excess (*i. e.*, until the fluid had a distinctly sweetish taste). This was made up to exactly 100 c.c. with water and filtered. After adding sodium phosphate in powdered form, sufficient to throw down the excess of lead, and once more filtering, 50 c.c. of the filtrate were put into a separator and shaken out with three portions of chloroform, dried and weighed, as in the first method.

Third Method.—After removing the lead by means of sodium phosphate, as in the preceding method, the alkaloid was precipitated by tannic acid, the liquid filtered off, the tannate washed and digested with lead oxide, this dried and the alkaloid dissolved out by means of alcohol, filtered. The filtrate again dried and weighed.

The result in each instance was as follows:

	Seed. Per Cent.	Root. Per Cent.
First method	0·9	0·6
Second method	0·6	0·4
Third method	0·4	0·4

Making for the seed an average of between 0·6 per cent. and 0·7 per cent.; for the root between 0·4 per cent. and 0·5 per cent. Therefore, it appears the seed are slightly richer in colchicine than the root, and should there be no other valid reason why the root should be retained in the Pharmacopœia, they would be sufficient whenever the effects of this drug are desired.

PENNSYLVANIA PHARMACEUTICAL ASSOCIATION.—The twenty-fourth annual meeting will be held at Hotel Oneonta, Harvey's Lake (near Wilkes-Barre), Pa., on June 18–20, 1901. Address the Secretary, J. A. Miller, Harrisburg, for orders for railroad excursion tickets.

CORRESPONDENCE.[1]

PROCTER MEMORIAL.

In response to a letter from the Editor of this JOURNAL concerning the feasibility of establishing a Research Laboratory as a memorial to the life and work of Prof. William Procter, Jr., by the American Pharmaceutical Association at its semi-centennial in 1902, the following are some of the replies which have been received:

DEAR SIR:—That a monument to the memory of Prof. Wm. Procter will be erected is now a practically established fact, judging from the letters that have appeared in the recent numbers of the AMERICAN JOURNAL OF PHARMACY, and the question remaining is to determine what form this memorial shall take.

The statue, the medal, the scholarship, the research laboratory, each has its advantages and its disadvantages. Of the four, it seems to me that the statue is the least desirable. In perpetuating the memory of such a man as Procter we want a *living* monument, something that will be ever before the minds of the pharmacists of to-day and of the future, something to stimulate us to do better work. If a statue be erected and placed in Washington, but a small percentage of pharmacists will ever hear of it again after its unveiling. Those who visit Washington may see it, but in that city of sights not more than one in a thousand would be sufficiently impressed to make him return home resolved to do more for the advancement of pharmacy.

The medal, granted once in three or five years so that it will not become too common, would undoubtedly stimulate quite a number, but it seems to me even then there would be a decided restriction in the amount of good accomplished.

The scholarship granted every year would help a larger number of men; but probably most of them to whom it would be given would be recent graduates, frequently young men not fully matured and consequently not equipped to produce the best results.

The research laboratory, if it can be properly equipped, manned and maintained (giving due weight to that "if"), would be the ideal memorial. It would be as lasting as the statue and far more impressive. The results of the labor done there would not appear only once in three or five years, but every year and several times a year, and it

[1] For other information and correspondence on this subject, see editorials, November, 1900, and February, March, April and May issues of this JOURNAL.

would not be the work of more or less immature men, but that of men who have already learned to work to the best advantage. Dr. Lyons' suggestions seem particularly good. If we could bring about such a condition of things, so that by law, or better, by public opinion, all medicinal substances to be deemed worthy of recognition by physicians must come up to the standard set by the laboratory, we would have done much for pharmacy. Make the stamp of the laboratory of sufficient value, so that manufacturers will be glad to have it on their goods, and those who are now putting out inferior articles, not bearing the stamp of the laboratory, would be stigmatized or driven from competition. This would, of course, be only a part of the work of the laboratory. Original investigations along practical lines should receive equal attention.

NASHVILLE, TENN. EDSEL A. RUDDIMAN.

DEAR SIR:—Replying to your recent favor; there is no question but what a pharmaceutical research laboratory under proper control and direction, whose work should be restricted to supplying data for the Committee of Revision of the Pharmacopœia and for working out improved formulas and methods of manipulation for semi-official products such as are included in the National Formulary, might be of great value to the profession of pharmacy and add very largely to the reputation of American Pharmacy as compared with its past record.

To be of value a strong committee should be selected, consisting of chairman and able members of the Committee of Revision of the Pharmacopœia, the President, Permanent Secretary, Chairman of the scientific section and of the dispensing section of the American Pharmaceutical Association, and all work done should first have the sanction of this body.

It would seem that the establishment of such a laboratory in connection with some government institution at Washington, as the laboratory of the Department of Agriculture, would be more economical and advantageous than to equip and conduct an entirely independent institution. If all the expenses were borne, it might be feasible to make some such arrangement and it might not.

BOSTON, MASS. E. L. PATCH.

DEAR SIR:—Replying to your request for further comments on the proposed Procter Memorial, I will say that a careful reading of

the suggestions made in the February, March and April editions of the JOURNAL leaves me still of my original opinion—that the best memorial that can be devised will be a research laboratory in the city of Washington. Of course such would be a large undertaking, but by no means as expensive as some predict. The $200,000 plant suggested by one of your contributors would be magnificent, but its magnificence would be chiefly in the direction of extravagance. Twenty to thirty thousand dollars would suffice, and beyond that sum expenditure is hardly necessary. A stately palace of marble with superb equipment would be expensive, I grant; but do we plain pharmacists need such a structure? Would the plain Quaker whom we wish to honor desire such a monument? No! Let us aim at something simple; let our motto be "Deeds rather than dazzle;" let the Procter Memorial Laboratory become known by the achievements of its workers rather than by the gorgeousness of its façade. President Garfield's famous saying relating to the teaching capacity of Mark Hopkins, his statement that a log cabin and a bench with his revered teacher at one end and the student at the other, was preferable to a college with magnificent equipment and poor teachers, is justly applicable in the present case.

Surely, it were an infinitely better monument to Procter to have a modest building and equipment with zealous workers, than a massive pile with nothing done.

Let a similar case be cited: The Lloyd Library is, or should be, the pride of American pharmacy. Its complete equipment is a positive joy to all engaged in research work, and its fame has gone forth to the furthermost parts of the pharmaceutical world. What matters it that it is housed in a modest building, with naught but a little tablet announcing its purpose. Its fame comes from its usefulness, not from its personal appearance.

Therefore my idea is that a research laboratory should be started, even though only $15,000 were raised. Let a modest house be purchased in Washington, and equipped for pharmacopœial research work. If the work emanating from the institution is valuable, it will surely grow to greater things, and (as a judicious investment in Washington realty rarely depreciates) as further funds are forthcoming, the first modest home might be sold and a more pretentious plant erected. For, let it be said in passing, the writer does not urge a cheap monument to the "Father of Ameri-

can Pharmacy," he merely deprecates efforts to discourage modest beginnings.

CLEVELAND, O. H. V. ARNY.

DEAR SIR:—I am heartily in sympathy with the movement to establish a suitable memorial to Professor Procter. After reading the various ideas expressed in the A.J.Ph., I have slightly modified the opinion which I had first formed.

If it were possible to raise sufficient funds for the proper equipment and maintenance of a research laboratory my ideal would be accomplished. As I doubt very much that this can be carried into effect my second choice would be a fellowship. In case this would not be feasible then a Procter medal to be bestowed only once in two or three years for continuous, exceptionally meritorious work along pharmaceutical lines is the least, in my judgment, that should be decided upon.

ANN ARBOR, MICH. J. O. SCHLOTTERBECK.

DEAR SIR:—In reply to yours of the 4th inst., I desire to say that I am in entire accord with the research laboratory idea, providing the project can be carried out in an adequate and generous way. This it seemed to me at first not easily possible, but if the indications now point to a greater probability of accomplishment, the movement would have my fullest support. There ought to be a liberal endowment for maintenance or some other arrangement that would from the beginning remove the need of that practice of economy that is never fruitful.

I will be glad to do what I can to help the matter along.

MINNEAPOLIS, MINN. FREDERICK J. WULLING.

DEAR SIR:—Your favor of the 4th inst. to hand and noted. I am decidedly in favor of establishing a research laboratory as a memorial to Professor Procter, and think it decidedly the most suitable and desirable memorial we could erect to him. But I fear it will be too great an undertaking, and that the maintenance of it will be more than the A.Ph.A. can finance. The first expense will perhaps be too large for practical purposes even, for I cannot see where the funds will come from. The fixed charges after it is erected then will be in excess of what it can earn in my judgment, and we cannot depend or look with any assurance upon governmental support or maintenance. If it is located in New York City,

it may earn more from the many importers, who may avail of its facilities, than it would if located at Washington, but in any event I fear it cannot be successfully carried out by the A.Ph.A. The erection of the Hoffmann Haus in Berlin required great and long-continued efforts on the part of the chemists and chemical industries of the world, and we cannot hope to enlist the interest of nearly so many people, nor nearly so many large and wealthy industries. While hence I would prefer to see a research laboratory be the memorial for Professor Procter, I think the most that the A.Ph.A. can hope to successfully carry out is a gold memorial medal to be awarded annually to the pharmaceutical chemist or botanist that has in the judgment of a suitable committee advanced the science the most during the year.

BALTIMORE, MD. A. R. L. DOHME.

RECENT LITERATURE RELATING TO PHARMACY.

THE DISTILLATION PRODUCTS OF CASTOR OIL.

It has been often noticed that toward the end of the distillation of castor oil, the residue in the retort very suddenly and with development of considerable gas is converted into a sticky rubber-like mass. H. Thoms and G. Fendler (*Arch Ph.*, 1901, 1) report examination of the residue, which they find consists largely of the glyceride of a dibasic fatty acid, triundecylenic acid $(C_{11}H_{20}O_2)_3$.

From this glycerine the anhydride of the acid was isolated in the form of a bright yellow, somewhat elastic mass, having the formula $C_{33}H_{58}O_5$ which corresponds to the composition $(C_{11}H_{20}O_2)_3-H_2O)$. The residue on heating with potassa yielded a new acid of the oleic acid series, a body melting at 36° and of formula $C_{16}H_{30}O_2$.

H. V. ARNY.

CONCERNING OIL GLANDS.

An important contribution to the study of plant processes is an article with above title by A. Tschirch and O. Tunman (*Arch. Ph.*, 1901, 7.)

The special subject investigated was the method of secretion of resins, or of oils, or of gums in the various glands or secretion cells, the work being performed by aid of microscope and appropriate stains. Among the latter the Unverdorben-Franchimont reagent,

(copper acetate 1 part, water 20 parts) is given the preference, it staining resins from blue to emerald green, according to botanical origin. Passing over the individual peculiarities of each resin and oil-bearing plant examined, we find the following important conclusions:

First: In no case were volatile oils and resins found in the secretion cells, bordering the intercellular spaces of the stems, the contents of such cells being either of fat or of tannin. Ethereal oil is invariably found in subcuticular spaces (hence in glands), where it evidently originates, being decomposition product of the cell wall rather than of the cell contents.

Second: Wherever resin is found, mucilage accompanies it; the walls of resin glands invariably having a mucilaginous layer in which, according to the writer, the resin is manufactured; in other words, the layer which Tschirch calls "resinogenous" (resinogene schicht) is invariably mucilaginous.

Third: As yet the exact chemical processes involved in the origin of resins and oils is unknown.

Fourth: It is observed that while tannin accompanies the resins in most glands, it is found more abundant in old glands than in young ones. This fact could be construed either as favoring or disproving the theory that tannin is an intermediate stage in the formation of resins. The writers lean toward the affirmative opinion, explaining the deficiency of tannin in the young cells by saying that it is all used up in the process of transformation into resin and that when the glands become older and the resin formation ceases, the unused tannin is stored up without change. H. V. A.

CONCERNING CATHA EDULIS.

This plant, a native of Abyssinia and Arabia, where it is called Kat and where its leaves have been used from the earliest times by the natives of that region as an innocent stimulant, such as our coffee and tea, is the subject of a lengthy paper by A. Beiter (*Arch. Ph.*, 1901, 17.) Passing over his pharmacognostical description we find that he obtained from the plant an alkaloid by treating the leaves with chloroform, saturated with ammonia, evaporation of the chloroform, solution in acidulated water, extraction with chloroform and repeated crystallization. The yield was about $\frac{7}{100}$ of one per cent., was in the form of small needles of bitter un-

pleasant taste and with no odor. It gave reactions with the usual alkaloidal precipitants and likewise responded to the common color tests. It possesses alkaline reaction and assayed to the formula $C_{10}H_{18}N_2O$. From the leaves was also obtained an interesting rubber-like product, melting at 120°, dissolving in carbon disulphide and other caoutchouc solvents and also vulcanizing. It analyzed to the formula $C_{10}H_{17}O$. There was also isolated from the leaves considerable tannin, seemingly representative of both the iron green and iron blue classes. Lastly was obtained mannite and an ethereal oil lighter than water, and smelling like tea. The ash of the leaves, 11·59 per cent. consisted of magnesium, calcium, iron, chlorine, sulphates and carbonates.

The seeds of the plant on extraction with petroleum ether yielded 50 per cent. of fixed oil. H. V. A.

CASCARA AND ITS ADULTERANTS.

A form of adulteration of cascara sagrada not likely to be met with in this country is reported from France (E. Perrot, *J. Ph. et Ch.*, 1901, 161). It is the addition of buckthorn bark, and the article deals with the pharmacognosy of the two drugs in the form of powder, the conclusions being that the chief difference between buckthorn and cascara sagrada is that the former never contains sclerotic cells (a characteristic of the latter), and is always of a red-brown color rather than a yellow-brown. H. V. A.

CHEMISTRY OF FRESH KOLA NUTS.

The reason of the superiority of the fresh kola nut over the dried is explained as due to the fact that kola contains an oxidizing ferment which utilizes the oxygen of the air in converting the kola alkaloids as well as the coloring matter into insoluble forms. This is in line with the recent investigation on the so-called oxydases, the careful study of which is certain of explaining many of the causes of deterioration now unknown. Thus, it is stated that the darkening of all fruit on drying, and also the relative inferiority of a dried fruit to a fresh one, is due to the presence of such oxidizing ferments, which produce a chemical change on all fruit exposed to the air. Fresh kola nuts contain a normal and soluble alkaloid, called kolanine, which under the influence of the oxidizing ferment is decomposed or rendered insoluble. Sugar, however, prevents such

deterioration, hence it is highly advisable to dispense the kola in the fresh form, either as a saccharine, fruit pulp, as a syrup, or as an elixir. As to the so-called kola red, there is much confusion concerning this product, at least three distinct bodies bearing this name, and all of these are supposed to be pathological products produced by the oxidizing ferment. Hence, the attempt to judge the value of kola nuts by amount of kola red they obtain is characterized as absurd.—(Charles, *Bull. de Sc. Pharmacol.*, 1900, 495, through *Schw. Woch. Ch. u. Ph.*, 1901, 25.) H. V. A.

ACTION OF METALS ON 95 PER CENT. ALCOHOL.

95 per cent. alcohol of neutral reaction and leaving no residue on evaporation was left in contact during six months, placed in bottles of white glass, carefully corked with each of the following metals: Copper, iron, tin, lead, zinc and galvanized iron. At the end of six months the originally clear liquid was found turbid and containing quite a residue other than the metal itself, and the alcohol from each of the metals save copper, yielded on evaporation a decided amount of residue. Unfortunately, the experiment was not a quantitative one; however, it leads to the valuable conclusion that all metals used, with the exception of copper, are partly soluble in alcohol. (Dr. Malmejac, *J. Ph. et Ch.*, 1901, 169). H. V. A.

ESTIMATION OF SUGAR IN URINE.

The administration of methylene-blue obscures the Fehling's test in the urine of the patient. In such cases the urine must first be decolorized by aid of solution of mercuric nitrate; subacetate or acetate of lead not answering the purpose.—(G. Patein, *J. Ph. et Ch.*, 1901, 172.)

A NEW SYNTHESIS OF THE ALCOHOLS.

Treatment of an alcohol with its sodium salts yields an alcohol having twice the number of carbon atoms. Thus inactive amylic alcohol $C_5H_{12}O$ with its sodium derivative, yields an alcohol $C_{10}H_{22}O$. Likewise onanthic alcohol $C_7H_{16}O$ plus its sodium salts yields Beta-dionanthic alcohol $C_{19}H_{30}O$ and the onanthate of sodium. Likewise the dionanthic alcohol heated with the sodium derivative of onanthic alcohol gives trionanthic alcohol $C_{21}H_{44}O$. The two new bodies, dionanthic and trionanthic alcohol, are described in the article.—(M. Guerbet, *J. Ph. et Ch.*, 1901, 179.) H. V. A.

MANNA FROM THE OLIVE TREE.

In the gardens of Mansourah near the Iron Gate of the Danube, there are some very ancient olive trees, the trunks of which yield abundantly of manna, some of the exuding pieces weighing almost a kilo. The product on examination yielded 52 per cent. of mannite, identical with that from the manna ash. The residue consisted of sugar, gummy matter, debris and water.—(J. A. Battandier, *J. Ph. et Ch.*, 1901, 177.) H. V. A.

EDITORIAL.

CHARLES RICE.

Without knowledge that Dr. Charles Rice had been ill, the pharmaceutical world was startled by the announcement of his decease on Monday morning, May 13th, at 10 o'clock, in his apartments at the Bellevue Hospital, New York City. The fact was, he had not been well all winter, and few apprehended even during his last hours that the end was at hand. As recently as May 8th, he had sent out to the members of the Committee of Revision of the U.S.P., several circulars bearing on the work. On Saturday afternoon, May 11th, he went out for a drive in Central Park, but on returning was compelled to go to bed, from which he never arose. As to what was the cause of his death, it is not entirely apparent, it being supposed that he died of aneurism of the aorta. On May 3d he wrote: "It looked at one time as if I had to drop all work not absolutely incumbent upon me, but there is enough improvement visible to justify me holding on at least for a while longer, until it can be seen what the summer will do for me. I first had the grippe, and this was followed by intercostal neuralgia and indications of asthma, which, some weeks ago, became very annoying. But I am getting better, and am only kept back by the unfavorable weather."

Dr. Rice was of Austrian parentage, and was born on October 4, 1841. Of his early life and subsequent career until he came to this country we know little, save that he received a very thorough education in the classics, mathematics and the languages in various schools in Munich, Passau and Vienna. Having been disappointed in obtaining a position requiring a knowledge of Sanskrit under the

British Government, he came, through the influence of an uncle, to America, in 1862. During the war he served in the navy as hospital steward, and had an opportunity of visiting various foreign countries. After his discharge from service he had a spell of illness and was taken to Bellevue Hospital. Meanwhile he was made assistant to John Frey, the apothecary of this institution, and prosecuted his chemical studies so that upon the death of the latter he was made superintendent of and chemist to the general drug department of Bellevue Hospital, and subsequently chemist to the Department of Public Charities and Corrections of New York City, which positions he held during the remainder of his life.

His later life has been so rich in accomplishments that a knowledge of all the details of his early life are not essential to an understanding of his character. His whole life was devoted to high purposes and was so filled, in not only doing his own work, but also in giving aid and counsel to others, that when one approached him there was no time for gossip or idle chat. Indeed, it would not be saying too much that these things were foreign to his nature, and that life had a greater meaning for him than this. It seems almost as though Emerson must have been writing of some such personality as his when he portrays what a friend should be, and says:

"Why should we desecrate noble and beautiful souls by intruding on them? Why insist on rash personal relations with your friend? Why go to his house or know his mother and brothers and sisters? Why be visited by him at your own? Are these things material to our covenant? Leave this touching and clawing. Let him be to me a spirit—a message, a thought, a sincerity. A glance from him I want, but not news nor pottage. I can get politics and chat and neighborly conveniences from cheaper companions. Should not the society of my friend be to me poetic, pure, universal and great as nature itself? Ought I to feel that our tie is profane in comparison with yonder bar of cloud that sleeps on the horizon, or that clump of waning grass that divides the brook? Let us not vilify, but raise it to that standard. * * * * Worship his superiorities."

Dr. Rice was one whom it will require years to appreciate and understand. He will undoubtedly rank as the superior of all who have labored before him in the profession of pharmacy. "He taught, as the artist must, without intention, and his lesson was how a man may be modest and self-reliant." In reply to a request for a biographical sketch, he sent the following on March 11, 1900:

Concerning your last letter, I want to say now that I beg you to give up the idea of making any sort of display of me in print. The older I get, the more distasteful is this to me. I cannot prevent any one from acting on their own will and judgment, but when I have a chance of giving my views *before* the thing is done, I trust that my wishes will be fulfilled. My life, before I came to this country, passed along in so uneventful a manner that the only landmarks in it that I could point to, are fully covered by the biographical sketch in the *American Druggist* some seven or eight years ago. Since I am here, and since I hold my present position in the Department of Public Charities (now about thirty-four and one-half years) my connection with pharmaceutical journalism and pharmacopœial matters are, I believe, sufficiently well known not to require announcement. Whatever is to be said about me, let it be said after I am gone. Any sort of display about me, particularly now, would be surely taken by some persons as a personal advertisement on the eve of the convention. I am sorry that Dr. ———— has seen fit to put such a puff into ————————, yet I cannot blame him, as he did not know how I feel about it.

Hoping that you will drop the idea and comply with my wishes, I remain your sincere friend,

CHARLES RICE.

A close study of the life of Dr. Rice will show that he was pre-eminently a man of character. One could not but see in him the personification of all the noble traits. He, unlike other men, apparently had no chart or compass. He simply acted and lived as seemed best, and what he did was right. He was so unselfish in all his actions that he amazes us, and was with difficulty sometimes understood. In 1885, as Chairman of the Committee on Unofficial Formulas of the American Pharmaceutical Association, he had worked out a plan whereby the New York and Brooklyn Formulary, which he and others in the vicinity of New York had made so successful, was to be turned over—for the sake of the larger field of usefulness and greater good—to become the property of the American Pharmaceutical Association. The discussion on this subject (see Proc., 1885, pp. 558–564 and 574–575) is most interesting reading. The proposition was at first refused, and then through Mr. Ebert the matter was again brought up and Dr. Rice spoke as follows. Those who knew Dr. Rice can doubtless see him and hear him, because the tenor of his remarks on this occasion were characteristic of him on all occasions. He said:

Mr. President:—Certainly, yesterday it appeared to me that there was a peculiar reluctance, to accept the gift freely offered, but I am happy to say that reluctance due to a misunderstanding has been overcome. This may have occurred in reading the report hastily. We had in substance offered you the

following terms: We have asked you to approve of the Formulary, provided you thought it worthy. That was the proposition, or, perhaps, merely a suggestion on the part of the committee. Then the other proposition was put in the form of an invitation from the New York and Brooklyn societies, asking the Association to join in the copyright. We did not insist that you should copyright it; we offered it to you and wanted to help you in the matter of getting the copyright, as we are incorporated. Or if you did not want it copyrighted, and are rich enough to put your hand into your pocket and pay for its publication without insuring to yourselves the exclusive sale of it, you could go ahead and do it. The next proposition was that we ask you—actually ask you—to take all the work that had been done in the preparation of the third edition, which we interrupted in order to make you this offer. We did not ask you to appoint us a committee. As a committee you can appoint anybody else. We are very willing to turn over all our papers to this committee. We knew that some money was required to carry on the experiments, and we suggested that you place some funds at the disposal of the committee. You need not do this if the committee are all rich men and are willing to pay the expense themselves. But you could not expect everybody to do that and serve upon the committee. If this committee is going to correspond with the State pharmaceutical associations in all parts of the United States, to find out what formulas each one desires to have introduced, with a view of making them uniform, there will be some expense. In view of the fact that all the work would cost something, we suggested that you set aside for the use of the committee $250.

It should not be forgotten that a previous committee made an official request of our General Committee to let them have the New York and Brooklyn Formulary, in order to incorporate it in their report to this Association, because they could not get up anything better. We made the reply that we were not authorized at the time to turn over the book; but as the work has now advanced so far in our hands, we concluded to give it to the Association in order to make it national. We sent a representative to Philadelphia to see the Council, and the Council seemed to be satisfied with the offer at that time so far as they understood it; but they decided that they were not authorized to accept it, or to act in the premises, and the advice then given us was to come to the Association. In response to that invitation, we make you a very liberal offer and that is what was given to the Association yesterday. Yesterday the impression on my mind and on the minds of my colleagues was very strong that our offer was supposed to be not quite disinterested, and that for this reason cold water was thrown upon it. I am glad to say that that was a misapprehension. The explanation made a little while ago is satisfactory, and the offer still stands, without any reserve of any kind; and if you are ready to act upon it, we shall be perfectly satisfied.

This was the beginning of the National Formulary, and in its inception, principles and subsequent policies Dr. Rice was the master hand.[1] For most men this would have been a monumental

[1] See Proc. A.Ph.A., 1884, p. 506; 1885, pp. 558, 574; 1886, pp. 159, 177, 191; 1887, p. 496; 1888, first issue of the National Formulary.

work. But even a greater work was done by him on the U. S. Pharmacopœia. To wholly grasp the dilemma and appreciate the position of the pharmacists of the United States in regard to the revision of the Pharmacopœia and the needs of reform, one must consult the Proceedings of the A.Ph.A. for 1876 and 1877.[1] Suffice it to say that in endeavoring to solve the difficulties, one of our foremost pharmacists said of his own plan and efforts (Proc., 1877, p. 531): "The design and plan which was presented to the Association last year has been entirely and, I was going to say, ignominiously defeated. * * * The American Medical Association has distinctly refused to have anything to do with the subject, and now we are in the condition we were in before the broaching of the subject. The subject was entirely mine; brought up entirely by me, originally in the American Medical Association, and so far as I am concerned, it has been entirely defeated and entirely frustrated. * * * The whole subject of the Pharmacopœia seemed to me to require reconstruction and reform, and I undertook that subject with hesitation, but yet earnestly and carefully and with the least possible personality, and proposed a method of reform and a plan for discussion. This soon brought upon me and my propositions an amount of abuse of a character so personal and so intemperate as to be extremely disagreeable, and therefore, I am now ready to leave the matter and turn my attention to something better than setting up for a reformer, even though still convinced of the necessity of the reform."

It was under these circumstances that Dr. Rice was asked to serve as chairman on the Special Committee of the A.Ph.A. on Revision of the U.S.P. In the following year he organized the committee, distributed the work among members and others, and was ready to report at the meeting in 1878 (see Proc., p. 668) a developed and successful plan. The work completely broke down his health, and he asked to be relieved therefrom. This was done, and it was then that Professor Maisch said (see Proc., p. 879) that "it is principally due to that energy and wonderful talent of organizing possessed by Mr. Rice that it [the work on the Pharmacopœia.—Ed.] has reached its present advancement." In closing his report, Dr. Rice said, in his customary manner: "The chairman is grateful

[1] See Proc. A.Ph.A., 1876, pp. 629–650; 1877, pp. 531–539. 552–557.

for the honor conferred upon him, as well as for the expressions of encouragement which he has received during the past year; but it should be borne in mind that all the advance thus far made is primarily due to the able and earnest workers who are members of the committee, or who have assisted the committee in its labors." Notwithstanding his modesty, Professor Maisch at that time showed upon whom the honor should be placed, and for twenty years the pharmaceutical and medical professions have recognized that it was the character and intellect, the mind and heart of Charles Rice that pre-eminently made the U.S.P. what it is to-day. Fortunately he lived long enough to mould the policies and direct the work of revision of the forthcoming Pharmacopœia, so that the success of it is assured. His place cannot be filled, but his influence on pharmacopœial work, like that on the National Formulary, has been so great that for all time men will know what to do and how the work should be done. He made the compass and the chart, and while difficulties will present themselves and storms will arise, yet there surely must be those who will be familiar with his life and actions so that all will be well in the future, and the U.S.P. will continue to hold its own for all time to come.

Dr. Rice never posed as the reformer; he knew too well the experiences of men from the time of Confucius to Emerson; that what was needed was the work that the present generation required to be done. He, knew, too that this required the co-operation of every one who could contribute to it. He knew who could work and he had them work. He organized and led; and every one else received the honors and emoluments for the work. He was satisfied that the work was done. When the convention of 1890 voted him an honorarium of $1,000, he turned it back into the Revision Committee Fund to pay others for their labors. As chairman of the Revision Committee of 1900 he was voted a salary, but he never asked for it and had not, we believe, been paid for his services. He was the ready worker at all times, doing his own work and that of others too. If the needed work required him, it mattered not the condition of his health or how much other work he had to do, he was ready to do it. When on account of impaired health he asked to be relieved of the chairmanship of the Committee of Revision of the A.Ph.A. in 1878, and after the chairman who succeeded him had resigned, and after several ineffectual attempts to induce other mem-

bers of the Committee to accept the position had failed, he (see Proc., 1879, p. 668), "rather than let the whole plan fail for want of an organization, consented, much against his wish, to re-accept the office on the authority of the Executive Committee and of the President." The entire report is well worthy of perusal, as it shows this man of modesty and self-assurance in a strength and beauty that is most commendable.

Dr. Rice wrote a great many papers, and he never wrote unless he had something of value to say. What many investigators would have put into an elaborate paper he put simply into a statement of fact, as is shown in his answer to the query on "The asserted variable solubility of sulphate of morphia" (see Proc., 1875, 821), of which there is not even a record in the general index. In this connection it may be stated that he was Associate Editor of *New Remedies*, which was subsequently merged into *The American Druggist*. He served as chairman of the Committee on Adulterations and Sophistications of the A.Ph.A. in 1873 and 1874, and demonstrated how useful this committee might be in collating personal observations, private communications and published reports in the various journals bearing on this subject. These reports will always be deserving the careful perusal of committees having this matter in charge, as the disposition of the work, the general deductions and observations, hold as true to-day as then. Dr. Rice served the A.Ph.A. on many occasions. When through failing health Professor Diehl was compelled to resign as Reporter on the *Progress of Pharmacy*, Dr. Rice though not present was elected to help the association out of its dilemma. He arranged for the work, divided the salary among those whom he engaged to assist him in it, arranged the report for the press, read the proof, and even made the index himself. Surely no man in pharmacy acted like this man, giving his time, his money and himself on each and every occasion. He was First Vice-President of the A.Ph.A. at the meeting in Washington in 1883 and doubtless would have been made President of the semi-centennial meeting in 1902.

Dr. Rice was an active member of the College of Pharmacy of the city of New York and was chairman of the Committee on Examinations. He also served the College in other ways; as chairman of the Library Committee and as a member of the Board of Trustees, and in the language of Samuel W. Fairchild, former President of the

College, "was unfailingly and devotedly interested in the affairs of the College and zealous in promoting every measure that seemed to promise improvement in the College work."

All that has been referred to in this brief sketch is but a part of the career of this great man, and was the work accomplished during his period of recreation. His best work was given as chemist and superintendent to the Department of Correction and Charities of New York City. He conducted all this work without permitting the political rings in New York City to influence it in the least; he organized the work and made the department the only one that has not suffered through the influence of political intrigue at one time or other. He so conducted his department that, though the work might be scrutinized with all the malice of a foe, nothing should reward the search but the finding of a faithful adherence to duty.

And yet when all this is said we have but glanced at the personality of this man. He was an unusual scholar and master of a dozen or more of languages. He was a most thorough linguist and recognized as an authority on questions of philology and etymology and was one of the foremost Sanskrit scholars in this country. He was a proficient mathematician, and had a thorough grasp of recent researches in both theoretical and physical chemistry. He was a chemical as well as a biological analyst and was on the staff in the Pediatrics Laboratory in New York City. He had a working knowledge of botany and zoology that simply amazed specialists in these branches. At one time he was doing microscopical work in these sciences, and at another, systematic work. No one comprehended this man in his entirety. To each he revealed a part of himself, and because his attainments in a particular field stood out in such bold relief, men did not comprehend that he was equally accomplished in others, and so men have compared their notes and they each find that he stood for more than they thought; and now that the work of collating the facts of his life, his achievements and his character has begun, they like the hues of the opal and the light of the diamond, will become more and more apparent as we come together and speak of him and write that record.

Dr. Rice was an Honorary Fellow of the New York Academy of Medicine and Honorary Member of the following organizations:

British Pharmaceutical Conference, Philadelphia College of Pharmacy, Maryland College of Pharmacy, German Apothecaries' Society of the City of New York, the Alumni Association of the Philadelphia College of Pharmacy, and the following State pharmaceutical Associations: Louisiana, New Jersey, Ohio and Pennsylvania. He was a corresponding member of the following societies: Société de Pharmacie d'Anvers, Colegio de Pharmaceuticos di Barcelona, Sociedad de Historia Natural de Mexico, Pharmaceutical Society of Athens (Greece) and of the Société de Pharmacie de Paris.

He was a Regular Member of the German Oriental Society of Leipzig und Halle, the American Oriental Society, the New York Academy of Science, the New York Botanic Garden, the American Chemical Society, the American Pharmaceutical Association, the College of Pharmacy of the City of New York, the Committee of Revision of the United States Pharmacopœia, etc.

He received the following honorary degrees: Doctor of Philosophy from the University of the City of New York, and Master in Pharmacy from the Philadelphia College of Pharmacy.

There is but one father of American pharmacy as there is but one "father of his country." These honors cannot be shared. But as the name of Abraham Lincoln in American history, so the name of Charles Rice will endure in the history of American pharmacy. Each, like a meteor, has his own path of glory, and each, like the famous mountain peaks, serve as resting places for our ascending footsteps that we may catch the inspiration to do our part and do it well. Dr. Rice, by reason of his attainments of intellect and character, "indisputably enjoyed an elevated rank in human nature." One ventures to believe that an adequate memorial of him will some day be undertaken. Meanwhile his memory is safe; his work will be conserved and his example we should endeavor to emulate.

PHARMACEUTICAL MEETING.

The last of the series of pharmaceutical meetings of the Philadelphia College of Pharmacy for 1900-1901 was held Tuesday, May 21, 1901. Dr. Adolph W. Miller, Corresponding Secretary of the College and Lecturer on Materia Medica at the University of Pennsylvania, presided. There was a fair attendance, and in other respects the meeting was a fitting close to the series of meetings.

The first speaker was Mr. F. B. Kilmer, New Brunswick, N. J., who read a most interesting and exhaustive paper, entitled "A Story of Papaw." (See p. 272.) Mr. Gordon stated that some years ago, when stationed at Colon, on the Isthmus of Panama, on board the Atlanta, the crew were supplied with salt pork, salt fish and beef, the physician in charge ordered them to get a supply of papaw and wrap the meats in the leaves over night, which rendered them digestible, and as a result the crew were very free from sickness.

In reply to questions by Professor Lowe, Mr. Kilmer said that the natives rub the meat with the papaw and then also boil it with the meat, and that the ferment acts until the boiling point is reached when it is destroyed. Mr. Kilmer said that while it might seem plausible to cut off the fruits and then incise them, this was not found to be practicable as the latex flows but a very short time only after the fruit is removed from the tree.

In reply to the question of Mr. Boring as to whether the custard apple, sometimes found in this region, is the same as the papaw to which Mr. Kilmer referred, Mr. Kilmer stated that the papaw did not occur further north than Jacksonville, Fla., as it will not stand the frost, and Dr. Miller stated that the plant to which Mr. Boring referred is the *Asimina triloba*, an entirely different plant.

Referring to certain portions of the paper, Professor Kraemer said in speaking of the variability of seeds which necessitates a selection on the part of the planters of papaw, that this is due to the fact that all the seeds, even though produced in the same pod or in the same fruit, are not necessarily alike, because each does not receive the same amount of nutriment and hence do not have the same degree of vitality. In this connection he referred to recent investigations which showed that the different commercial varieties of strophanthus were not necessarily derived from different species, but might be obtained from the same species, the difference being due to the position in the pod, those more remote from the direct supplies of food being less, or improperly, developed. He also mentioned the fact that pistillate plants of *Arisæma triphyllum* deprived of the proper amount of nourishment produced the following year staminate plants.

Professor Kraemer also referred to the subject of natural indicators (see this JOURNAL, p. 174) and thought that the color principle

to which Mr. Kilmer referred belonged, in all probability, to this class of substances, which were apparently of rather wide occurrence in nature. He also referred to a recent paper in *Science* (see p. 765), in which the author points out the living character of the ferments.

Frederick T. Gordon read a paper on "Notes on the Use of Methyl Alcohol in Pharmacy" (see p. 285). In the discussion Mr. Wiegand pointed out that the odor in wood alcohol can be removed by passing the electric current through it. Dr. Miller said that it was sometimes used in making bay rum, and that he could always detect the odor, which was very offensive to him. E. Fullerton Cook, Assistant Director of the Pharmaceutical Laboratory, presented some abstracts of recently published articles referring to "The Use of Methyl Alcohol in Pharmaceutical Preparations" (see p. 289). Frederick T. Gordon presented some "Notes on the Spoliation of Syrups," which will be printed in a subsequent issue of this JOURNAL. F. W. Haussmann sent some notes bearing on this question, which will also be published later. Dr. Miller stated that broken rock-candy cost, by the barrel, about 1 cent more per pound than granulated sugar, and that the cost of rock-candy would therefore not interfere to any considerable extent with its use in the preparation of medicinal syrups. Mr. Boring favored Mr. Gordon's suggestion to make syrups in quantity to suit the demand for them. Mr. Boring further said that he used rock-candy in making syrup of hydriodic acid, and that in the preparation of syrup of wild cherry he used the finely powdered bark, which he placed loosely in the percolator. He moistens the bark, pours it into the percolator, allows it to macerate, then removes, moistens again and pours back into the percolator, the extraction then being rapid and satisfactory.

A device for cutting soap, by V. Clyde Michels, was exhibited, which consisted of a ruled board with a wire attached, so that the soap can be cut off in definite sizes. Mr. Boring stated that he heated the soap on a register and cut it with an ordinary spatula. Dr. Lowe suggested that several pieces of wire should accompany the apparatus, as the wire was likely to break, and that he found it necessary to buy a large quantity in order to have it on hand.

On motion of Mr. Boring, which was seconded by Dr. Weidemann, a vote of thanks was tendered the speakers for their communications.

H. K.

PERSONAL NOTES.

THE MONUMENT TO PASTEUR, which is to be erected in his native town, represents, besides a statue of Pasteur, a figure personifying science, who is holding a wreath of laurel toward Pasteur and a woman holding two small children, who are supposed to have been saved from death by Pasteur's discoveries.

A MEMORIAL MARBLE BUST OF ROBERT BROWN, the eminent botanist, has been unveiled in the picture gallery of Marischal College, the University of Aberdeen.

WALTER MYERS' CHAIR OF TROPICAL MEDICINE has been endowed in the Liverpool School of Tropical Medicine, in memory of the late Dr. Myers, whose life was sacrificed in the study of yellow fever.

EMIL BEHRING, Professor of Hygiene and the History of Medicine at Marburg, has had conferred on him on the occasion of the bi-centenary of the Prussian monarchy, the patent of hereditary nobility.

MAX VON PETTENKOFER, Professor in the University of Munich and the eminent authority on hygiene and bacteriology, committed suicide on February 10th, fearing that he would become insane, which fear seems to have been well grounded as the autopsy subsequently showed.

THEODORE HUSEMANN, Professor of Pharmacology and Toxicology of the University of Göttingen, died unexpectedly on February 13, 1901.

HENRY C. BLAIR, a prominent apothecary of Philadelphia, Pa., died on January 7, 1901, after a brief illness.

WILLIAM R. WARNER, senior member of the firm of Wm. R. Warner & Co., manufacturing pharmacists, died April 3, 1901, of apoplexy.

HANS M. WILDER, well known for his ability in preparing indices, in translating and abstracting scientific literature, and in arranging scientific collections, died on January 25, 1901.

A PORTRAIT OF W. W. KEEN, the eminent surgeon and professor in the Jefferson Medical College, Philadelphia, has been presented to that institution by his colleagues and students.

G. A. HANSEN, the discoverer of the lepra bacillus, will have his sixtieth birthday on July 29th celebrated by the erection of a marble bust, in the Lungegaard Hospital, Bergen, where he discovered the bacillus.

THE RÖNTGEN SOCIETY OF LONDON offers, as a gift from its President, a gold medal to be awarded to the maker of the best X-ray tubes.

CHARLES F. CHANDLER, President of the College of Pharmacy of the city of New York, has been appointed by the President a member of the U. S. Naval Observatory.

THE LIST OF THE HONORARY MEMBERS in the Philadelphia College of Pharmacy has been increased by the recent election to membership of Prof. Dr. Arthur Meyer, Marburg, Germany; Dr. B. H. Paul, London; Dr. Charles Rice, New York City (since deceased); Helen A. Michael, Boston; Dr. Charles T. Mohr, Asheville, N. C.